**Abstract**

A grating-coupled waveguide (GCW) and a method are described herein that can be used to detect the presence of a biological substance (e.g., cell, drug, chemical compound) in a sensing region of the GCW. The GCW includes a substrate, a diffraction grating and a waveguide film that has a higher index of refraction than the substrate which has an index of refraction $\leq 1.5$. The relatively low-index substrate effectively increases the sensitivity of the GCW by causing the waveguide mode to shift towards a biological substance located in a sensing region above the waveguide film, thereby increasing the field strength of the mode's evanescent tail in this region. In one embodiment, an array of the GCWs are incorporated within the wells of a microplate.